

# Calf Bioimpedance Ratio Improves Dry Weight Assessment and Blood Pressure Control in Hemodialysis Patients

Yi-Lun Zhou Jing Liu Fang Sun Li-Jie Ma Bin Han Yang Shen Tai-Gen Cui

Department of Nephrology, Chao-Yang Hospital, Capital Medical University, Beijing, China

## Key Words

Blood pressure • Calf bioimpedance ratio • Dry weight • Hemodialysis

## Abstract

**Background:** Chronic fluid overload due to overestimation of dry weight (DW) is the major factor in the development of hypertension in hemodialysis (HD) patients. **The present study was undertaken to investigate whether bioimpedance ratio in the calf (Calf-BR = impedance at 200 kHz/impedance at 5 kHz) could be a useful hydration marker for estimation of DW and facilitate better control of blood pressure (BP) in HD patients.** **Methods:** Target range of Calf-BR was derived from 157 healthy Chinese subjects. Post-dialysis Calf-BR was measured in 117 stable, non-edematous HD patients. Those with Calf-BR(s) above target level had their DW(s) gradually reduced under the guidance of Calf-BR. **Results:** The Calf-BR was normally distributed and increased with age, but was independent of BMI and gender in both healthy subjects and dialysis patients. HD patients with Calf-BR above age-stratified target range had significantly higher home BP, in spite of more antihypertensive treatments ( $p = 0.058$ ). The patients who reached the target range of Calf-BR by decreasing DW, had their home BP significantly decreased, along with reduction in antihypertensive medications ( $p = 0.012$ ). **Con-**

**clusion:** Recognition and correction of chronic fluid overload based on age-stratified Calf-BR is helpful in hypertension control in Chinese HD patients.

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## Introduction

Hypertension is prevalent in hemodialysis (HD) patients and is an important cardiovascular risk factor [1, 2]. Aggressive control of hypertension in dialysis is mandatory. Extracellular fluid overload is the most important factor leading to hypertension, and may contribute to the high prevalence of left ventricular hypertrophy (LVH) observed in HD patients [3]. The major goal of HD treatments is to remove excess fluid targeted to attain 'dry weight (DW)', which is defined as the lowest tolerated post-dialysis weight achieved via gradual change in post-dialysis weight at which there are minimal signs or symptoms of either hypovolemia or hypervolemia [4]. In most instances, DW is estimated clinically by trial and error, the consequence of which is that about 50% of HD patients who have achieved clinically determined 'ideal' DW are actually hypervolumic [5]. Although the reduction of DW is documented to be a simple and efficacious maneuver to improve blood pressure (BP) control in hy-

pertensive HD patients [6], excessive ultrafiltration due to absence of precise DW assessment may predispose the patient to intradialytic hypotension, cramps and increased risk of access thrombosis. In addition, volume overload is an important but not the only determinant of hypertension in HD patients. Therefore, accurate assessment of the hydration state of HD patients by other alternative methods is very much needed, and recognition of volume-related hypertension may facilitate better BP control by removal of excess fluid.

Bioelectrical impedance (BI) offers the potential as a simple and relatively inexpensive technique for the assessment of volume status. Different approaches such as whole-body or segmental BI have been used to measure extracellular volume (ECV), total body water (TBW) in dialysis patients [7, 8]. However, how to derive the normohydration weight from BI measurements has not yet been described.

It is documented that under physiological conditions, the ratio of ECV to TBW remains tightly regulated, and an alteration in this ratio reflects a change in ECV. In biological tissues, lower frequency currents travel preferentially in the extracellular space, whereas high frequency currents traverse both ECV and intracellular volume (ICV) [9]. The ratio of impedance at a high frequency to impedance at a low frequency will increase when the ratio of ECV to TBW increases, since impedance measured at a high frequency inversely correlates with TBW, as impedance at a low frequency does with ECV. Although impedance ratio is not the exact ratio of ECV to TBW, it could reflect the tendency of changes in ECV to TBW, and therefore could be used as a surrogate marker of ECV.

In the current study, we tested the usefulness of calf bioimpedance ratio (Calf-BR) in determining volume status and the efficacy of DW reduction based on Calf-BR in BP control in Chinese HD patients.

## Method

### Subjects

HD patients were recruited when: (1) they had been on HD for more than 3 months; (2) they had had no clinical cardiovascular disease during 3 months preceding entry into the study; (3) they had no known acute inflammatory event, malignant disease, and the serum albumin >30 g/l; (4) they had no chronic liver disease and chronic obstructive pulmonary disease, and (5) they had no pitting edema in either leg before HD. The subjects were registered between May 2009 and June 2009. All patients were dialyzed 3 times weekly and 4 h for each treatment session, with polysulfone hollow-fiber dialyzer (F7, Fresenius Medical Care AG). All

patients were dialyzed with a bicarbonate-buffered dialysate (sodium 138 mmol/l, potassium 2.5 mmol/l, calcium 1.5 mmol/l, magnesium 0.5 mmol/l, bicarbonate 32 mmol/l). Blood flow rate was individualized from 200 to 300 ml/min. Dialysate flow rate was 500 ml/min. Dialysate temperature was 36.5°C. A Kt/V >1.2 was required. The study was approved by the institutional review board, and written informed consents were signed by all patients.

117 HD patients were recruited in this study. The causes of renal failure were chronic glomerulonephritis (40 patients), interstitial nephritis (25 patients), primary hypertension (19 patients), diabetes (17 patients), polycystic renal disease (5 patients), chronic pyelonephritis (5 patients), and unknown (6 patients).

157 apparently healthy subjects without a history of cardiovascular or renal disease or diabetes or liver disease were enrolled for defining a target range of Calf-BR for HD patients.

### Multifrequency Bioimpedance Measurement

A multifrequency bioimpedance spectrum analyzer device (BodyStat, UK) was used to measure impedance in right calf at 4 frequencies (5, 50, 100, and 200 kHz) at the sitting position after sitting for 20 min. Four electrodes were placed on the calf, one at ankle, one at the third metatarsophalangeal joints, one at inferior border of patella, and one at 5 cm lower than inferior border of patella. Each set of BI data would be retrieved from the average of the two runs of measurements. In HD patients, the measurement was performed 30 min after the end of a midweek dialysis session (Wednesday or Thursday). Calf-BR was calculated as follows: Calf-BR = impedance at a frequency of 200 kHz/impedance at a frequency of 5 kHz.

### DW Reduction Based on Calf-BR

Target ranges of Calf-BR were arbitrarily defined as age-stratified mean  $\pm$  1 SD of Calf-BR value obtained from healthy controls (details as shown in Results). The HD patients whose Calf-BR(s) were above the age-stratified target range were recruited in the prospective trial. DW was gradually decreased by 0.2–0.3 kg per session or every other session, or per week until the Calf-BR reached the target or persistent symptoms occurred, such as hypotension, muscle cramps or nausea, etc. The period of DW reduction was set to be 2 months in the present study. BP (both clinic and home) was closely monitored during the period. Average BP in 1 week before starting or after 2 months of DW adjustment were taken to represent the BP at start and at end point.

### Blood Pressure Measurement

Pre- and post-HD BP measurements were recorded at each visit by the dialysis unit personnel using a standard technique after at least 5 min rest and using a validated oscillometric device (HEM 7052, Omron Healthcare). Three readings at each point were averaged to provide one recording. During HD sessions, BP was monitored every hour.

Home-monitored BP was analyzed. All patients were trained to measure their BP at home three times daily – on waking up, between noon and 6 p.m., and at bedtime, using a validated self-inflating automatic oscillometric device (HEM 7052 or 7112; Omron Healthcare). Patients were advised to take one measurement at rest after sitting for at least 5 min and to record their BP readings on a provided data sheet. Three BP recordings during 1 day were averaged to provide one recording. Averaged home BP over 1 week was recorded. The prescription of antihypertensive thera-

py based on home-monitored BP, and episodes during and after dialysis, was evaluated at every HD visit, and adjusted by nephrologists every week.

Current clinical guidelines call for monitoring home BP for the diagnosis of hypertension and management of all patients with hypertension [10, 11]. One week averaged home systolic BP of  $\geq 150$  mm Hg [12], which has the best combination of sensitivity and specificity to predict hypertension diagnosed by the gold standard of ambulatory BP monitoring, was used to diagnose uncontrolled hypertension in HD patients.

### Clinical Information

Parameters were recorded for analysis including number of antihypertensive medications, pre- and post-HD body weight using an electrically calibrated scale, ultrafiltration volume and rate, body mass index (BMI) which was calculated according to the formula:  $BMI = \text{weight}/\text{height}^2$  ( $\text{kg}/\text{m}^2$ ). Episodes were recorded such as dyspnea, weakness, nausea, muscle cramping, and hypotension during the intradialytic or interdialytic periods. In the case of antihypertensive medication, a unit dose was recommended by the manufacturer in order to provide a measure of equivalence between different agents [13]. Since the majority of patients were receiving different antihypertensive agents, particularly at baseline, the total number of dose units was calculated for each patient to facilitate comparison.

### Statistical Analysis

Data was expressed as the mean  $\pm$  SD. The Student's t test or paired t test was used for unpaired or paired samples. Differences between more than two groups were analyzed using ANOVA and post-hoc Scheffé test.  $\chi^2$  test was used to analyze non-parametric data. Correlation was determined by linear regression analysis. Statistical analysis was performed using SPSS for Windows release 11.5 (SPSS, Inc., Chicago, Ill., USA), and significance was defined as  $p < 0.05$ .

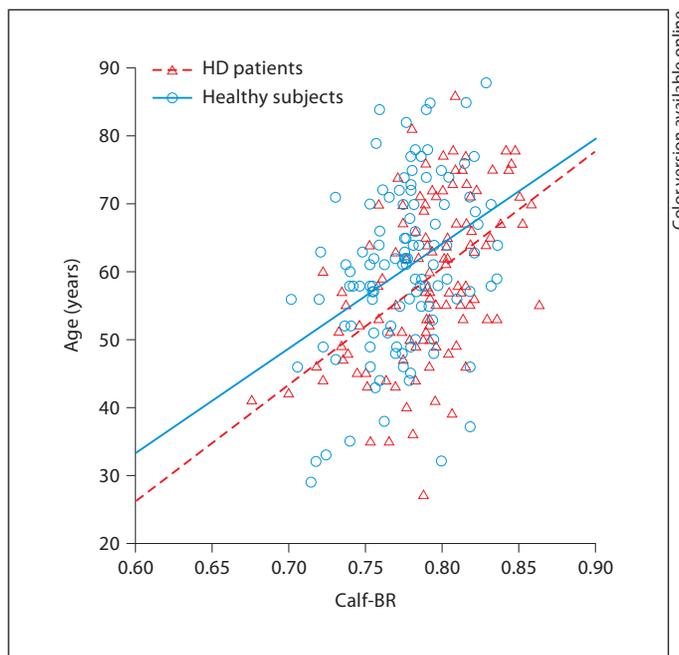
## Results

### Distribution of Calf-BR

The Calf-BR showed a normal distribution in both healthy subjects and HD patients. There was no significant difference between males and females ( $p = 0.143$  in healthy subjects,  $p = 0.787$  in HD patients). The Calf-BR increased progressively with age in both groups ( $r = 0.269$ ,  $p = 0.001$  in healthy subjects;  $r = 0.486$ ,  $p < 0.001$  in HD patients) (fig. 1), but was constant over the entire range of BMI ( $r = -0.139$ ,  $p = 0.083$  in healthy subjects;  $r = -0.110$ ,  $p = 0.238$  in HD patients).

### Target Range of Calf-BR for HD Patients

The Calf-BR(s) in healthy subjects were divided into three groups by age: young group (18–44 years), middle-aged group (45–64 years), and elderly group ( $\geq 65$  years). Age-stratified mean  $\pm$  1 SD for Calf-BR in healthy con-



**Fig. 1.** Correlation between Calf-BR and age ( $r = 0.269$ ,  $p = 0.001$ , in healthy subjects;  $r = 0.486$ ,  $p < 0.001$  in HD patients).

**Table 1.** Age-stratified descriptive values of Calf-BR from healthy subjects and HD patients

	Healthy subjects	HD patients	p value
Young (18–44 years)	n = 26	n = 14	
Age	38.7 $\pm$ 5.0	39.6 $\pm$ 4.8	0.593
Calf-BR	0.769 $\pm$ 0.030	0.759 $\pm$ 0.037	0.375
Middle-aged (45–64 years)	n = 95	n = 65	
Age	55.2 $\pm$ 5.6	55.3 $\pm$ 5.9	0.895
Calf-BR	0.771 $\pm$ 0.028	0.786 $\pm$ 0.031	0.002
Elderly ( $\geq 65$ years)	n = 36	n = 38	
Age	74.4 $\pm$ 5.8	72.4 $\pm$ 4.5	0.114
Calf-BR	0.787 $\pm$ 0.024	0.809 $\pm$ 0.025	<0.001

Calf-BR = Impedance ratio in the calf; HD = hemodialysis. Values are arithmetic mean  $\pm$  SD.

trols and HD patients were listed in table 1. We assumed the range of age-stratified 1 SD from mean Calf-BR in the controls, as the target range for the corresponding HD patients. 42 patients had Calf-BR(s) above target range, suggesting a hypervolemic state. 63 patients had Calf-BR(s) within target range and 12 patients had Calf-BR(s)

**Table 2.** Comparison of the incidence of hypervolemia among three groups according to age

	Calf-BR above target range	Calf-BR within or below target range
Young (n = 14)	1 (7%)	13 (93%)
Middle-aged (n = 65)	24 (37%)	41 (63%)
Elderly (n = 38)	17 (45%)	21 (55%)

Calf-BR = Impedance ratio in the calf; HD = hemodialysis. Values are presented as the number of patients. Percentage of patients in parentheses.  $p = 0.042$ .

**Table 4.** Comparison of the characteristics between diabetic and non-diabetic patients

	Diabetic (n = 34)	Non-diabetic (n = 83)	p value
Age	62.8 ± 8.9	57.4 ± 12.6	0.010
Calf-BR	0.803 ± 0.031	0.785 ± 0.033	0.007

Calf-BR = Impedance ratio in the calf. Values are arithmetic mean ± SD. Age-adjusted Calf-BR(s) were still significantly higher in diabetic, compared to those in non-diabetic patients ( $p = 0.008$ ).

**Table 3.** Comparison of the characteristics among three groups according to Calf-BR target range

Calf-BR	Above target range (n = 42)	Within target range (n = 63)	Below target range (n = 12)	p value
Age	63.0 ± 9.6*	57.9 ± 12.8*	50.8 ± 8.4	0.003
Male/female	20/22	25/38	6/6	0.648
Body weight	61.91 ± 10.98	61.99 ± 10.20	64.35 ± 9.80	0.754
Body mass index	23.44 ± 3.68	23.93 ± 3.41	24.59 ± 3.43	0.572
Duration of dialysis, months	55.7 ± 46.6	47.0 ± 43.4	37.7 ± 22.8	0.376
Ultrafiltration volume, kg	2.35 ± 1.00	2.39 ± 1.11	2.81 ± 0.94	0.395
Pre-HD systolic BP, mm Hg	152.3 ± 27.9	143.1 ± 26.0	140.6 ± 22.9	0.165
Pre-HD diastolic BP, mm Hg	80.1 ± 13.8	78.3 ± 14.8	74.2 ± 15.9	0.457
Pre-HD mean BP, mm Hg	104.2 ± 16.3	99.9 ± 17.3	96.3 ± 13.6	0.256
Post-HD systolic BP, mm Hg	146.0 ± 20.4*	135.0 ± 21.1	128.9 ± 16.7	0.008
Post-HD diastolic BP, mm Hg	73.9 ± 9.7	73.0 ± 14.5	72.4 ± 10.0	0.897
Post-HD mean BP, mm Hg	97.9 ± 11.8	93.6 ± 14.5	91.3 ± 9.5	0.156
Home systolic BP, mm Hg	151.7 ± 19.5*,#	135.8 ± 18.8	129.9 ± 16.9	<0.001
Home diastolic BP, mm Hg	78.6 ± 11.3	76.4 ± 11.0	75.2 ± 10.8	0.499
Home mean BP, mm Hg	103.0 ± 12.7*,#	96.2 ± 11.7	93.4 ± 11.6	0.007
Uncontrolled hypertensive individuals	25 (59.5%)*,##	21 (33.3%)	2 (16.7%)	0.005
Antihypertensive medications	2.27 ± 2.14	1.47 ± 1.33	1.48 ± 1.80	0.058
Diabetic	20 (47.6%)*,##	13 (20.6%)	1 (8.3%)	0.003

Calf-BR = Impedance ratio in the calf; HD = hemodialysis; BP = blood pressure. Values are arithmetic mean ± SD, or values are presented as the number (percentage) of patients.

\*  $p < 0.05$ , \*\*  $p < 0.01$ , compared to the group with Calf-BR below target range.

#  $p < 0.05$ , ##  $p < 0.01$ , compared to the group with Calf-BR within target range.

below target range. In young HD patients, Calf-BR(s) were similar to those in age-matched healthy subjects ( $p = 0.375$ ). However, Calf-BR(s) were significantly higher in the middle-aged ( $p = 0.002$ ) and elderly group ( $p < 0.001$ ) on dialysis.

The incidence of hypervolemia was different among three groups by age ( $p = 0.042$ ), higher incidence was found in elderly patients compared to that in young and

middle-aged, although did not reach statistical significance (table 2).

Compared to the group with Calf-BR within or below target range, the group with Calf-BR over target range had significantly higher home systolic BP, higher percentage of uncontrolled hypertensive individuals, regardless of more antihypertensive medications ( $p = 0.058$ ), as well as higher percentage of diabetic (table 3).

**Table 5.** Comparison of characteristics at baseline and after 2 months of DW adjustment in HD patients reaching the target range (n = 27)

	Baseline	After DW adjustment	p value
DW, kg	59.4 ± 11.2	58.5 ± 10.9	<0.001
Calf-BR	0.822 ± 0.016	0.783 ± 0.017	<0.001
Pre-HD systolic BP, mm Hg	155.9 ± 29.7	141.1 ± 29.9	0.007
Pre-HD diastolic BP, mm Hg	81.7 ± 11.9	76.3 ± 13.5	0.022
Pre-HD mean BP, mm Hg	106.5 ± 16.4	97.9 ± 17.5	0.006
Post-HD systolic BP, mm Hg	145.0 ± 21.9	136.0 ± 19.4	0.030
Post-HD diastolic BP, mm Hg	75.1 ± 9.0	71.2 ± 11.8	0.034
Post-HD mean BP, mm Hg	98.4 ± 11.9	92.8 ± 13.0	0.021
Home systolic BP, mm Hg	151.7 ± 20.2	136.8 ± 19.9	<0.001
Home diastolic BP, mm Hg	79.6 ± 11.8	72.9 ± 10.0	0.001
Home mean BP, mm Hg	103.6 ± 13.2	94.2 ± 12.1	<0.001
Uncontrolled hypertensive individuals	20 (74.1%)	9 (33.3%)	0.001
Antihypertensive medications	2.49 ± 2.47	2.00 ± 2.28	0.012

Calf-BR = Impedance ratio in the calf; BP = blood pressure; DW = dry weight. Values are arithmetic mean ± SD, or values are presented as the number (%) of patients.

However, 23 patients with uncontrolled hypertension had Calf-BR within or even below target range.

After adjustment for age, Calf-BR(s) were still significantly higher in diabetic, compared to those in non-diabetic patients (p = 0.008) (table 4).

#### *DW Reduction under Guidance of Calf-BR*

Two patients moved away from Chao-Yang Hospital during the period of DW adjustment. 40 patients (females:males = 22:18, age 39–78 years) finished the intervention study. 13 of the 40 patients with Calf-BR over the upper limit failed to reach the target range, because of intradialytic hypotension or muscle cramps. Among the 13 patients, 8 patients were diabetic and 7 patients were elderly. However, the BP was easier to control in 10/13 patients.

27 patients had reached their Calf-BR target range after DW reduction without increasing the occurrence of intradialytic adverse events. Table 5 reported the BP at baseline and after DW adjustment for pre-, post-dialysis and home-monitored in HD patients who reached the target range. In addition, the changes of antihypertensive medication doses were shown. The reduction in DW was  $0.96 \pm 0.61$  kg. The decrease in home systolic BP and diastolic BP from baseline to after DW adjustment was significant (p < 0.001 and p = 0.001, respectively). The percentage of uncontrolled hypertensive individuals also significantly diminished (p = 0.001), along with reduction in antihypertensive medications (p = 0.012).

#### **Discussion**

Hypertension has long been identified as an independent cardiovascular risk factor in HD patients [2]. Chronic fluid overload due to overestimation of DW is the most important factor leading to hypertension in HD patients. The evaluation of DW on patients' symptoms during and after dialysis, and (or) physical examination is not exactly reliable. Therefore, it is important to establish more objective, practical and accurate means for DW assessment, in addition to clinical evaluation, which could facilitate recognition of volume overload, and thus better BP control.

A number of different approaches have been proposed for non-clinical DW assessment, including determination of natriuretic peptides, measurement of inferior vena cava diameter by ultrasound and intradialytic relative blood volume monitoring. However, for reasons of simplicity, reproducibility, accuracy, and cost reasons, none of these parameters were routinely used as the standard technique in evaluation of DW [14].

BI is a non-invasive technique to measure body hydration state and has gained widespread interest, particularly in HD patients for its objectiveness and simplicity [15–17]. BI as a means to determine ECV or/and TBW has been validated by applying dilution methods as the gold standard [18]. Several approaches to DW determination using BI have been developed, such as whole-body BI techniques, segmental BI methods and the continuous calf BI spectroscopy. Whole-body BI provides a sum of

measurements from the arm and leg but neglects much of the trunk. Segmental BI is superior to whole-body BI [7], but no uniform segmental BI methodology has been fully established yet. Continuous intradialytic calf BI as a novel application of segmental BI, tracks dynamic changes to relative ECV during dialysis and seems to be a promising tool [19, 20]. However, the calf BI curve may be influenced by the change in patient's body position and by eating or drinking during HD session, and the ultrafiltration rate should be constant. Thus, this method would be ideal, but not clinically feasible.

The bioimpedance ratio was first proposed as a marker of hydration status by Park et al. [8]. In their study the DW(s) of new HD patients were stepwise adjusted under the guidance of the bioimpedance ratio in the right leg. The reference of bioimpedance ratio (impedance at 50 kHz/impedance at 500 kHz) was obtained from a group of chronic but stable HD patients already achieving DW. The new HD patients successfully achieved their DW(s) by this method. In the current study, some modifications were made on top of this method. Firstly, our approach was based on regional BI of calf. Because of gravitational forces, the lower limb was more likely to be overhydrated than other anatomical sites, and may thus represent the best single location to delineate total body hydration [21]. Furthermore, the calf resembled a cylinder with a mostly uniform geometric shape and satisfied the requirement for standard BI measurements. Secondly, the ratio of impedance at 200 kHz to impedance at 5 kHz in the right calf (Calf-BR) was measured. The current frequency of 5 kHz, but not 50 kHz, selected for estimation of ECV in our study, avoided penetrating into the ICV and confounding ECV and ICV [22]. Thirdly, the optimum range of Calf-BR for HD patients was derived from 157 healthy subjects, but not HD patients, since half of clinical judgement of 'ideal' DW in HD patients are actually hypervolumic [4]. The present study showed that Calf-BR(s) in healthy subjects were normally distributed, within a specific narrow range, did not differ between males and females, and was independent of BMI, so it was possible to obtain an accurate hydration marker by Calf-BR.

Lastly, age-stratified Calf-BR target range was established. The present study showed that Calf-BR increased with age both in healthy subjects and HD patients. Similar supportive evidence in previous studies showed the ratio of ECV/TBW by whole-body BI techniques increased with age in HD patients and (or) healthy controls [23–26]. Data on leg by segmental BI method provided similar result [8]. The possible reason may be that most of the water content drop with age occurred at the ex-

pense of ICV and reduction of ECV was much lower [27]. The normohydration line of the Calf-BR versus age in healthy individuals may correspond to the same characteristics in HD patients at the state of DW. Therefore, more accurate estimation of DW would be available based on age-stratified Calf-BR.

Higher home BP and higher percentage of uncontrolled hypertensive individuals were presented in the group with Calf-BR(s) over target range which indicated volume overload. Home BP was more strongly related to the gold standard of interdialytic ambulatory BP [12], and was a stronger determinant of LVH and all-cause mortality in HD patients compared to pre- or post-dialysis BP recordings [28, 29]. A decrease in Calf-BR by lowering DW produced a reduction in home BP, accompanied by diminished antihypertensive medications. This confirmed the role of excess volume in causing hypertension in HD patients, in agreement with the finding of previous studies that hypertension in the majority of dialysis patients was due to chronic hypervolemia [30].

In the current study, normovolemia, even hypovolemia, was presented in 23 uncontrolled hypertensive patients. It was important to note that non-volume-related mechanisms, such as sympathetic nervous system and renin-angiotensin-aldosterone system hyperactivity, endothelins, and prostaglandins etc., may participate in dialysis-related hypertension. Therefore, reduction of DW was not necessary for every hypertensive patients, and accurate evaluation of hydration state was essential in hypertensive HD patients. On the other hand, even in patients with hypervolemia, a lag time of several days or weeks between improvement of volume and the resulting BP response [31], may induce clinical judgement error in DW, and thus over-ultrafiltration, which may further stimulate the sympathetic system and renin-angiotensin-aldosterone system. Hence, a stepwise reduction of DW should be based on serial bioimpedance measurements.

A higher percentage of diabetic and elderly patients was presented in the group with Calf-BR over target range, and a substantial portion of these people were unable to decrease their DW adequately because of intradialytic hypotension or muscle cramping. It is well recognized that patients with LVH with impaired left ventricular diastolic function may become hypotensive during dialysis treatments yet have very high BP during the interdialytic period. In addition, impaired sympathetic nerve activity or abnormalities in venous compliance commonly presented in diabetics could also lead to hypotension. Therefore, BP levels may be misleading in patients with various forms of cardiovascular dysfunction

or in the presence of autonomic insufficiency, particularly in diabetic or elderly patients as mentioned above. For this reason, measurement of DW by BI is critical to differentiate between underhydration and cardiovascular origin, due to different treatment strategy required for each condition.

A limitation of the present study is that, since we did not have access to isotopic dilution techniques, we could not evaluate with confidence the accuracy of Calf-BR method. Nevertheless, the correlation between reduction in Calf-BR and following decrease in BP is noteworthy.

Another limitation is that the number of healthy subjects enrolled into the study was relatively small. Age-stratified Calf-BR target range may be 'population-specific', and should be obtained on a sufficient number of local healthy volunteers. Enlargement of normal controls may further increase the accuracy of age-stratified Calf-BR reference range.

Finally, DW derived from healthy subjects may not be attained in elderly patients, especially with diabetes, by

regular HD treatment of 12 h/week. This is probably due to vascular or cardiac insufficiency, although attainment of such DW could be available in majority of young HD patients. How to make Calf-BR clinically feasible in elderly patients should be further investigated, modification of dialysis time or frequency may be implemented with the goal of reaching the target. Experience from Tassin, France, showed that long dialysis treatments (8 h, three times weekly) could produce optimal volume control [32].

In summary, modification of bioimpedance technique by the measurement of impedance ratio in the calf (Calf-BR) was a simple and practical method in assessing body fluid status in Chinese HD patients, and recognition of chronic volume overload by this method facilitated better BP control. However, large-scale studies are needed to further validate the accuracy and to clarify the long-term clinical values of DW assessment by this approach on cardiac function and cardiovascular morbidity and mortality in HD patients.

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